REMARKS

In the final Office Action[1] mailed April 29, 2009, the Examiner rejected claims 1, 3, and 4 under 35 U.S.C. § 103(a) as being unpatentable over Quate et al. (U.S. Patent No. 6,203,983, hereafter "Quate") in view of Washizu et al. (IEEE Trans. Ind. Appl., vol. 26, pp. 1165-1172, 1990, hereafter "Washizu"), and in further view of Wachter et al. (U.S. Patent No. 5,445,008, hereafter "Wachter"), and in further view of Daraktchiev et al. (U.S. Patent No. 6,457,369, hereafter "Daraktchiev"); and rejected claim 2 under 35 U.S.C. § 103(a) as being unpatentable over Quate in view of Washizu, Wachter, and Daraktchiev, and in further view of Yamamoto et al. (U.S. Patent No. 5,268,571, hereafter "Yamamoto"). Claims 1-4 remain pending and under consideration.

Applicants respectfully traverse the rejection of claims 1, 3, and 4 under 35 U.S.C. § 103(a) as being unpatentable over Quate in view of Washizu, and in further view of Wachter, and in further view of Daraktchiev; and the rejection of claim 2 under 35 U.S.C. § 103(a) as being unpatentable over Quate in view of Washizu, Wachter, and Daraktchiev, and in further view of Yamamoto.

Claim 1 recites an interaction detecting method for detecting an interaction between a detecting material and a target material in a detecting part, the detecting part including a reaction area for performing the interaction and a cantilever having a surface treated to fix the detecting material thereto, the method comprising, for example:

> forming, in the reaction area, an uneven electric field concentrated at the treated surface of the cantilever;
>
> vibrating and exciting the cantilever by using a driving source;

[1] The Office Action contains a number of statements reflecting characterizations of the related art and the claims. Regardless of whether any such statement is identified herein, Applicants decline to automatically subscribe to any statement or characterization in the Office Action.

> detecting a vibration amplitude of the cantilever by measuring a voltage of a resistor or a piezoelectric layer coupled with the cantilever; and
>
> detecting the interaction by measuring the change of the natural frequency of the cantilever based on the interaction.

(Emphasis added). Quate, Washizu, Wachter, and Daraktchiev, alone or combined, fail to teach or suggest all the elements recited in claim 1.

I. THE CITED REFERENCES FAIL TO TEACH OR SUGGEST AT LEAST "DETECTING THE INTERACTION BY MEASURING THE CHANGE OF THE NATURAL FREQUENCY OF THE CANTILEVER BASED ON THE INTERACTION," AS RECITED IN CLAIM 1.

The Examiner asserted, "Quate teaches methods for detecting hybridization of target nucleic acids (fig. 1-4; col. 5-6, for example) comprising: . . . detecting hybridization based on a change in resonant frequency (col. 4, lines 25-40, for example)." Final Office Action at 3. This is not correct.

For example, Quate, at column 5, lines 14-16, discloses, "as shown in FIG. 1, the surface of a cantilever 110 is first prepared in order to be able to attach single strands of DNA," and at column 5, lines 22-25, discloses, "a binding partner or probes molecules, for example, single stranded DNA 120, are introduced onto one surface of the cantilever [110]." In addition, Quate, at column 5, lines 30-34, discloses, "[t]he reflected spot 170 of light is used to determine the relative position of the cantilever [110]. In other words, movement of the cantilever [110] can be determined by directly detecting the movement or angle of the reflected laser beam light," (emphasis added). Further, Quate, at column 5, lines 41-50, discloses:

> The response from this first deflection on the detector [150] is used as a reference to determine cantilever deflection, as further described. Next, sample analyte molecules, such as DNA is introduced to the surface of the cantilever containing single stranded DNA. The sample analyte molecules

> will hybridize with selected strands of DNA on the cantilever, as reflected at numeral 180 in FIG. 3. As a result, stress is induced on the cantilever which will cause the cantilever to deflect. More specifically, when hybridization occurs, surface pressure results by the addition of negative charges on the surface of the cantilever because DNA is a polyanion. In other words, hybridization causes more electrostatic charges to build up on the cantilever surface which tend to repel one another. (Emphasis added).

Accordingly, Quate at best discloses that hybridization of DNA molecules is detected by deflection of cantilever 110, which is caused by electrostatic charges accumulated on cantilever 110, and that such deflection of cantilever 110 is determined by directly detecting the position change of reflected spot 170 (i.e., the movement or angle of the reflected laser beam). Quate does not disclose vibrating cantilever 110, and thus cannot disclose measuring the change of the natural frequency of cantilever 110. The Examiner also acknowledged that Quate does not teach vibrating cantilever 110. Final Office Action at 3. Accordingly, Quate fails to teach or suggest, "detecting the interaction by measuring the change of the natural frequency of the cantilever based on the interaction," as recited in claim 1 (emphasis added).

The Examiner did not rely upon Washizu, Wachter, and Daraktchiev for such a disclosure. Accordingly, Washizu, Wachter, and Daraktchiev fail to cure the deficiencies of Quate. In view of the above, claim 1 is distinguishable over Quate, Washizu, Wachter, and Daraktchiev.

II. THE CITED REFERENCES FAIL TO TEACH OR SUGGEST "FORMING, IN THE REACTION AREA, AN UNEVEN ELECTRIC FIELD CONCENTRATED AT THE TREATED SURFACE OF THE CANTILEVER," AS RECITED IN CLAIM 1.

The Examiner stated, "Quate does not expressly teach forming an uneven electric field at the surface of immobilized oligonucleotides." Office Action at 3. To cure

the deficiencies of Quate, the Examiner cited Washizu and stated, "Washizu provides a supportive disclosure that teaches the application of an uneven electric field to immobilize and stretch DNA molecules (pg. 1166, section III, experimental method, for example)." Office Action at 3. Further, in a response to Applicants' arguments, the Examiner stated, "the examiner is not asserting that the electrode disclosed in Washizu could constitute a cantilever," and "Washizu is relied upon to demonstrate the application of an uneven electric field to surface immobilized polynucleotides." Office Action at 5. Washizu fails to cure the deficiencies of Quate.

Applicants submit that claim 1 recites "forming, in the reaction area, an uneven electric field concentrated at the treated surface of the cantilever," (emphasis added). Accordingly, claim 1 requires that the claimed uneven electric field be formed in the claimed reaction area and concentrated at the treated surface of the claimed cantilever.

Washizu, on page 1166, right column, lines 35-39, discloses, "DNA molecules from λ phage (Sigma, cat. no. D9768, 48.5 kbp (kilo-based-pairs)) are suspended in deionized water at a concentration of about 5 μg/ml, with the fluorescent probe DAPI at 0.5 ~ 1.0 μg/ml, and introduced onto the electrode gap, which is then covered with a glass lid," (emphasis added). In addition, Washizu, on page 1166, right column, lines 47-51, discloses, "[t]wo types of electrode shape are used, one is a parallel strip electrode with a spacing of 60 μm, and the other is a right-angle edge-to-strip electrode, whose minimum spacing is 70 μm. The former is intended to give a uniform field, and the latter a nonuniform field," (emphasis added). Further, Washizu, on page 1167, left column, lines 16-19, discloses, "[i]n the case of the edge-to-strip electrode, a similar

phenomenon is observed, but the molecules are attracted to the region near the edge, where the field is strongest, with their axes directed along the field line (Fig. 1(b))," (emphasis added).

Accordingly, Washizu at best discloses a right-angle edge-to-strip electrode capable of applying a nonuniform electric field to DNA molecules suspended in deionized water. In addition, Washizu merely discloses that DNA molecules are attracted to the region near the edge of the edge-to-strip electrode. Washizu does not disclose forming a nonuniform electric field to surface immobilized DNA molecules. Neither does Washizu disclose that the attracted DNA molecules are fixed to the edge of the edge-to-strip electrode. Moreover, the Examiner acknowledged that the electrode disclosed in Washizu cannot constitute a cantilever. Office Action at 5. Accordingly, Washizu fails to teach or suggest, "forming, in the reaction area, an uneven electric field concentrated at the treated surface of the cantilever," as recited in claim 1 (emphasis added), and thus fails to cure the deficiencies of Quate.

The Examiner did not rely upon Wachter and Daraktchiev for such a disclosure. Accordingly, Wachter and Daraktchiev fail to cure the deficiencies of Quate and Washizu. In view of the above, claim 1 is distinguishable over Quate, Washizu, Wachter, and Daraktchiev.

III. ONE OF ORDINARY SKILL IN THE ART WOULD NOT COMBINE THE CITED REFERENCES IN THE MANNER ALLEGED BY THE EXAMINER.

Applicants submit that the conclusions in the final Office Action pertaining to obviousness were not reached based on facts gleaned from the cited references and that, instead, disclosures of the present application were improperly used in hindsight to

reconstruct the prior art. Without hindsight of Applicants' disclosure, one of ordinary skill in the art would not combine the cited references in the manner alleged by the Examiner. For example, without disclosure of Applicants' claimed uneven electric field concentrated at the treated surface of the claimed cantilever, one of ordinary skill in the art would not combine Washizu with Quate in the manner alleged by the Examiner.

In addition, Applicants submit that reasonable expectation of success is required to support a conclusion of obviousness and that "[e]vidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." M.P.E.P. § 2143.02, quoting *In re Rinehart*, 531 F.2d 1048, 189 U.S.P.Q. 143 (C.C.P.A. 1976), emphasis added. In this case, there is no reasonable expectation of success to combine the cited references in the manner alleged by the Examiner.

As discussed above, Quate discloses that hybridization of DNA molecules is detected by deflection of cantilever 110, caused by electrostatic charges accumulated on cantilever 110, and that such deflection of cantilever 110 is determined by directly detecting the position change of reflected spot 170. In addition, as discussed above, Washizu discloses a right-angle edge-to-strip electrode capable of applying a nonuniform electric field to DNA molecules suspended in deionized water.

Accordingly, by combining Washizu with Quate in the manner alleged by the Examiner, a nonuniform electric field generated by the edge-to-strip electrode of Washizu would then apply to cantilever 110 of Quate, on which electrostatic charges are accumulated after hybridization. As a result, the nonuniform electric field of Washizu would unreasonably further deflect cantilever 110 of Quate and thus unduly influence the position of reflected spot 170 of Quate, thereby destroying the results

detected by detector 150 of Quate. For at least this reason, there is no reasonable expectation of success to combine Quate and Washizu in the manner alleged by the Examiner.

Further, Wachter, at column 2, lines 23-46, discloses:

> To illustrate the basic invention operating principles, reference is given to FIG. 1 wherein element 10 represents a piezoelectric transducer supporting the attached end of a microcantilever 12 fabricated of quartz or silicon, for example. Responsive to a master oscillator 14 drive signal 16, the microcantilever is driven by the piezoelectric transducer at a non-loaded resonance frequency. A laser beam 18 emitted by laser diode 19 is reflected from the clean underside of microcantilever 12. The sweep of such reflection 20 is detected by an optical detector 22 such as a photodiode. As the reflected beam 20 sweeps back and forth across the detector 22, it produces a repetitive signal 24 with a frequency proportional to the oscillation frequency 16 of the microcantilever. Photodiode signal 24 is amplified 26 and the sweep pulses counted over a predetermined time interval by a counting circuit 28. The interval count is the substance of signal 30 issued by counter 28. (Emphasis added).

Therefore, Wachter merely discloses vibrating microcantilever 12 and detecting the vibrating frequency of microcantilever 12 by counting sweep pulses of a laser beam.

Accordingly, by combining Wachter with Quate in the manner alleged by the Examiner, cantilever 110 of Quate would then be vibrated by piezoelectric transducer 10 of Wachter, and reflected spot 170 of Quate would then be sweeping about detector 150 of Quate or about optical detector 22 of Wachter. As a result, no deflection of cantilever 110 of Quate could be observed by detector 150 of Quate or by optical detector 22 of Wachter. For at least this reason, there is no reasonable expectation of success to combine Quate and Wachter in the manner alleged by the Examiner.

Moreover, Daraktchiev, at column 3, lines 56-59, discloses, "application of an electrical current from the source 6 through heating element 3 causes a mechanical

stress between the layers 3 and 4 of the actuator, thereby causing the cantilever [1] to bend," (emphasis added). As discussed above, Quate discloses that deflection of cantilever 110 is detected by the position change of reflected spot 170.

Accordingly, by combining Daraktchiev with Quate in the manner alleged by the Examiner, heating element 3 of Daraktchiev would unduly bend cantilever 100 of Quate, thereby destroying the results detected by detector 150 of Quate. For at least this reason, there is no reasonable expectation of success to combine Quate and Daraktchiev in the manner alleged by the Examiner.

In view of the above, the rejection of claim 1 under 35 U.S.C. § 103(a) as being unpatentable over Quate in view of Washizu, Wachter, and Daraktchiev is improper and should be withdrawn.

IV. DEPENDENT CLAIMS 2-4 ARE DISTINGUISHABLE OVER THE CITED REFERENCES.

Claims 3 and 4 depend from claim 1 and are distinguishable over Quate, Washizu, Wachter, and Daraktchiev at least due to their dependence.

Claim 2 depends from claim 1. Yamamoto fails to cure the deficiencies of Quate, Washizu, Wachter, and Daraktchiev. Accordingly, claim 2 is distinguishable over Quate, Washizu, Wachter, Daraktchiev, and Yamamoto.

V. CONCLUSION.

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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